I. REMARKS

A. Status of Claims

The following Table I sets forth the current status of the claims:

Table I

Claim No.	Status	Claim No.	Status	Claim No.	Status
1-3	Previously Cancelled	40-42	Currently Amended	85-86	Currently Amended
4	Currently Amended	43-54	Previously Cancelled	87-89	Previously Presented
5-6	Cancelled Herein	55	Cancelled Herein	90	Currently Amended
7-9	Currently Amended	56-57	Previously Cancelled	91-94	Previously Presented
10	Previously Cancelled	58	Cancelled Herein	95	Cancelled Herein
11	Currently Amended	59-60	Currently Amended	96	New
12	Previously Cancelled	61-70	Previously Cancelled	97	New
13-16	Currently Amended	71	Currently Amended	98	New
17-33	Previously Cancelled	72	Previously Presented		
34	Cancelled Herein	73	Currently Amended		
35-36	Currently Amended	74-78	Previously Presented		
37-38	Cancelled Herein	79	Currently Amended		
39	Previously Cancelled	80-84	Previously Presented		

Claims 4, 7-9, 11, 13-16, 35-36, 40-54, 59-60, 71-94, and 96-98 are pending in this Application. New Claims 96-98 are added herein. Claims 5-6, 34, 37-38, 90 and 95 are cancelled herein. Claims 1-3, 10, 12, 17-33, 39, 43-54, 56-57 and 61-70 were previously cancelled.

Old claim 34 is cancelled herein and New Claim 96 added n its place. New Claim 96 is fully supported by the specification. It is respectfully asserted that the new claim language merely makes clearer what is regarded as an embodiment of Applicants invention. The other

amendments to the claims are either of a minor cosmetic nature or are make the claimed subject matter more clear.

B. Extension of Time

Accompanying this Response is a Petition for Extension of Time (PTO/SB/22) for a 1-month extension of time as well as the required fee.

II. APPLICANT'S INVENTION

The present invention is directed to a biodissolvable "single dosage form" containing one or more active agents, wherein the shape of the dosage form maybe a pill, tablet, lozenge, or dragée, and wherein the dosage form is a mat or web of biodissolvable fibers containing a medicament which is produce by electrohydrodynamic (EHD) means. Applicant uses the term "biodissolvable" to mean capable of being dissolved or disintegrated in the mouth or on the tongue of a human being or other animal or on another wet surface such as the surface of the eye to deliver for example, a local anesthetic to the eye after surgery. Tablets manufactured in accordance with the invention may also be provided so as to be reconstituted in water for injection and administered by IV injection. The fibres may be formed using any suitable biologically acceptable or compatible polymer that is hydrophilic so that, on contact with a wet surface, it effectively dissolves or deliquesces becoming liquid by absorbing the water on or at the surface. Suitable polymers include food grade gelatins, polyvinyl pyridine, polyvinyl alcohol, polysucrose, other polysaccharides such as starch and cellulose and its derivatives,

III. REJECTION UNDER 35 USC §103(A)

A. First Section 103(a) Rejection

Claims 7-9, 11, 13-16, 34-40, 55, 58-60, 71-76, 78-83 and 85-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee (WO 98/03267) and Roche *et al* (US 5,215,755) in view of Kovacs *et al* (US 5,322,698).

1. The References

a). The Coffee Reference

Coffee (WO 98/03267) describes an apparatus and methods for the preparation of a fibrous, mat-like wound dressing. The wound dressing may be directly sprayed onto the wound or burn using a hand-held or portable electrohydrodynamic ("EHD") spraying device. The fiber mat must be biodegradable and/or bioresorbable and may contain a medicament e.g., an antibiotic or an analgesic compound.

The diameter of the fibers in the web or mat as well as the space (gaps) between the fibers in the web is very important. Typically, the diameter of the fibers will range from 10^2 to 10^4 nanometers. The polymer materials which may be used to form the fiber mats are collagen, fibrin, polyhydroxybutyric acid, polyvinyl alcohol, polyglycolic acid, polylactic acid and New Skin®. New-Skin® is a commercially available example of the product type (i.e., wound dressing) which is the aim of the Coffee invention. New-Skin liquid bandage dries rapidly to form a protective cover that is antiseptic, flexible, waterproof, and lets the skin breathe. It protects the wound by keeping out dirt and germs and provides protection against infection with an antiseptic.

Examiner reads the Coffee reference as teaching processes and apparatuses for forming material by electrohydrodynamic comminution and that the processes and apparatuses disclosed in the Coffee reference are capable of producing various solid and partially solid forms, such as fibers, fiber segments, fibrils, droplets, particles, webs, and mats and that the formed matter may also contain a biologically active ingredient.

What Examiner does not assert is that the Coffee reference teaches or describes Applicant's claimed invention which is to a method of making a biodissolvable tablet containing a medicament where the tablet rapidly dissolves, or disintegrates when placed on a moist surface such as the tongue or buccal pouch of a human or animal. Because the

Coffee reference fails to describe the particular method of making the rapidly dissolving medicament claimed herein, Examiner relies on the Roche and Kovacs references to fill the total lack of teaching provided by the Coffee reference.

b). The Roche et al Reference

The Roche *et al* reference (US 5215755) describes the production of a chewable tablet containing a medicament e.g., ibuprofen comprising coated granules. The coated granules individually comprise the medicament granulated with the following compounds: polyvinyl pyrrolidone, sodium starch glycolate, and sodium lauryl sulfate in a fluidized bed granulator to produce granules of varying sizes.

Once the bulk granulate is formed, the granules are placed in another fluidized bed granulator and a water-soluble coating of hydroxyethyl cellulose (HEC) or a mixture of HEC and hydroxypropyl methyl cellulose (HPMC) is sprayed onto the individual granules. The granules are then screened to obtain the desired particle size range. Finally, the coated granules are compressed into chewable tablets. The purpose of the coating is to mask the taste of the medicament. The coating also adds an element of mechanical flexibility during tablet compression.

The tablets described by the Roche reference are "chewable", not rapidly dissolving and are formed from an entirely different method than the tablets of Applicant. There is no teaching or suggestion in the Roche reference which would reasonably direct one skilled in the art of electrohydrodynamic processing to combine the teachings of Roche with the teachings of Coffee.

c). The Kovacs et al Reference

The Kovacs *et al* reference (US 5322698) describes a process for preparing a tablet or dragée containing as the active agent, an antiarrhythmic aminoguanidine compound which has a "monoclinic crystal structure" which makes the aminoguanidine compound sensitive to moisture, heat and light.

The tablets of Kovacs are prepared using conventional tableting method. The unique feature of Kovacs is that the monoclinic crystalline structure of the active is protected using a particular combination of the active drug substance ("ADS") homogenized with an anhydrous alkaline earth metal salt, microcrystalline cellulose, a binder (e.g. polyvinylpyrrolidone), a glidant (e.g., colloidal silicon dioxide), an antioxidant (e.g., ascorbic acid), and one or more conventional tableting aids such as an anti-adhesive agent, a lubricating agent or a filling additive. These latter excipients are added to aid in release of the tablets from the tableting mold or to aid in compression of the tablet while in the tableting mold.

The unique protective system for the aminoguanidine compound developed by Kovacs comprises homogenizing a defined amount of an anhydrous alkaline earth metal salt and microcrystalline cellulose along with the monoclinic moisture-, heat- and light-sensitive active ingredient. The use of this unique system prevents any increase in the free energy at the binding sites on the active ingredient, which could induce a chemical change, i.e. the decomposition of the active ingredient since the displacement at the binding sites of the mobile anions being present in the crystal structure of the active ingredient is inhibited by the alkaline earth metal salt and simultaneously, a tablet can be obtained which is suitably solid for coating, conveniently disintegrates in the stomach and advantageously releases the active ingredient.

Kovacs teaches that a coating may be applied to the tablets of his invention. Since the active ingredient is so water sensitive the coating must be applied in an organic solvent. The

coating contains a hydrophilic component (such as polyethylene glycol, water-soluble cellulose ethers or vinylpirrolidone/vinyl acetate copolymer) and a hydrophobic component (ethylcellulose or acrylate/metacrylate ester copolymer) dissolved or suspended in a pharmaceutically acceptable organic solvent. Kovacs teaches (Col 3, lines 36-40) that the "coat has to satisfy two demands: on the one hand, the active ingredient should be protected against the harmful effects of light and air moisture and on the other hand, a suitable dissolution of the active ingredient has simultaneously to be ensured."

The coating must not dissolve in the mouth but is designed to dissolve or develop cracks in the stomach so as to facilitate the release of the active ingredient in the stomach of the patient.

One skilled in the art of tableting would be taught little by the Kovacs reference except, perhaps the optimal tableting formulation for the specific aminoguanidine active agents described in the reference. There is nothing in the Kovacs reference which teaches anything about the preparation of tablets that immediately dissolve in the mouth.

B. Second Section 103(a) Rejection

Claims 4-9, 11, 13-16, 34-38, 40-42, 55, 58-60 and 71-95 rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee (WO 98/03267) and Roche et al (US 5,215,755) in view of Kovacs et al (US 5,322,698) as applied to claims 7-9, 11, 13-16, 34-40, 55, 58-60, 71-76, 78-83 and 85-95 above, and further in view of Hansen et al (US 6,423,346 B1).

1. The Hansen et al Reference

Hansen et al (US 6423346) describes and claims the preparation of a particular fish gelatin having a bloom strength above 100. The gelatin is prepared by a particle forming method which is either a spray gelation method or a double emulsifying method. The fish gelatin described by Hansen has unique physical properties with respect to resistance to

mechanical influences. The high mechanical strength of the fish gelatin of Hansen makes it very useful for the preparation of tablets which are compressed.

Applicant teaches that gelatin is one of the suitable hydrophilic polymers which may be used in the carrier liquid in method of the invention. However, the gelatin used by Applicant is not required to have unique physical properties. All it must do is dissolve in an appropriate solvent. It is not necessary that the gelatin used by Applicant in the methods of the invention have great mechanical strength because by its nature the fiber mat or web formed by EHD processes has a sturdiness or strength flowing from the fact that the fibers of the mat randomly overlay one another.

III. **APPLICANT'S ARGUMENTS**

One skilled in the art of electrohydrodynamic aerosolization or fiber formation would not look to the teachings of Roche, Kovacs or Hansen for any insight into the techniques, problems or methods relating to EHD aerosolization or fiber formation. Examiner states that, "... one of ordinary skill in the art could combine the collective disclosures of the prior art with a reasonable expectation of success." This begs the question, success of what?

By Examiner's own admission, the Roche reference is cited only to show sweeteners and flavorings are known in the "art". Applicant readily admits it is well known that many drugs have a bitter or unpleasant taste and that it is common in the preparation of oral dosage forms to mask the bitter or unpleasant taste of the active agent by adding a flavoring or sweetening agent.

If, as Examiner specifically states, the Roche reference is cited merely to show that sweeteners and flavorings are known in the art. What "reasonable expectation of success" is Examiner talking about? If a sweetener or flavoring is added to the wound dressings of Coffee one killed in this art would still not achieve Applicant's claimed invention.

Examiner goes on the state that , "Coffee and Roche meets claims limitation as stated above but fails to include vinylpyrrolidone/vinylacetate copolymer as biologically acceptable polymer in the process of manufacturing tablets." It is respectfully, asserted that neither Coffee nor Roche disclose Applicants claimed method or the biodissolvable tablets produced by that method.

It is true that Kovacs discloses a process for the preparation of a tablet or dragée composition. However, the so-called "rapid absorption" described by Kovacs refers to absorption of the active agent in the stomach of the patient taking the tablet. Because the active aminoquanidine described by Kovacs is heat-, moisture- and light-sensitive the tablet composition and the coating have to perform the unique functions relative to the active agent described above. The tablets of Kovacs are formulated to protect the active agent from heat and moisture in the tablet composition while the coating must protect the active from light and humidity and also allow the active agent to dissolve through the coating in the stomach.

The tablets of the present invention almost instantly dissolve when they come in contact with moisture on the tongue or in the buccal pouches. On the other hand, the tablets of Kovacs do not instantly dissolve in the mouth much less in the stomach. It would likely take at least 20 minutes in the stomach for the tablets of Kovacs to release significant active agent.

The Coffee reference does not teach or describe Applicant's claimed invention. Clearly, Examiner recognizes that this is the case because Examiner looks to Roche, Kovacs and Hansen to fill this lack. The problem with this is that these references are not remotely related to EHD aerosolization or EHD fiber formation.

Examiner uses the cited references to show bits and pieces of Applicant's invention; e.g., the use of a sweetener and a flavoring in a tablet (Roche); the use of vinylpyrrolidone/vinyl acetate copolymer as a coating for the tablets (Kovacs); and a particular fish gelatin (Hansen). All of these ingredients (excipients) are well known to the pharmaceutical formulator and the pharmaceutical formulator is well aware of standard references which describe the use of such excipients in various

solid dosage forms. See for example, Remington's Pharmaceutical Sciences, The United States Pharmacopeia (USP),2008 McCutcheon's Emulsifiers and Detergents: North American Edition, and 2008 McCutcheon's Functional Materials: North American Edition.

It is irrelevant that a particular component of Applicant's tablets is known in the art. Applicant does not claim any particular excipient *per se*. The question is whether there is a logic provided by the cited reference or by common knowledge which would lead one skilled in the art of EHD processing of aerosols and/or fibers to modify the teachings of Coffee to the degree necessary to arrive at the invention claimed herein.

By Examiner's own admission, the Roche reference does not do this. The Kovacs reference describes a tablet tailored for a particular heat-, light- and moisture sensitive active agent. While the teaching of Kovacs would teach something to one skilled in the art trying to formulate an active drug substance with the same issues, the disclosure of Kovacs would not even be considered relevant by Roche because it teaches nothing about making a chewable tablet. Finally, Hansen describes the preparation of a particular fish gelatin. To what end? What does Hansen teach to one trying to make a rapid dissolution tablet that dissolves on the tongue?

If the world of science is a big "haystack" full of knowns, the mere fact that one may find all of the elements of one's invention in the "haystack" does not make the invention obvious. The prior art has to provide a reason to reach into the haystack and select the particular elements that form the invention; otherwise, everything is obvious.

IV. CONCLUSION

Based on the amendments and arguments made herein, it is respectfully asserted that Examiner's rejections under 35 USC §103(a) have been overcome and that this Application is in condition for allowance. Examiner is respectfully requested to withdraw all rejections and to issue a Notice of Allowance. If there are any questions regarding these amendments and remarks, Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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Date: February 16, 2009

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